MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

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INTEROFFICE COMMUNICATION

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November 9, 2015

To: File for Antimony Trisulfide Sb_2S_3 (CAS No. 1345-04-6)

From: Mike Depa, Toxics Unit, Air Quality Division

Subject: Initial Threshold Screening Level

Previously, the averaging time (AT) assigned to antimony trisulfide was 24 hours, as per the default methodology (Rule 232(2)(b))(see attached memo from Dan O'Brien dated April 27, 1998). The current file review concludes that the AT may appropriately be set at annual, based on the nature and duration of the key study and the ITSL value derivation, as allowed under Rule 229(2)(b). Therefore, the AT is set to annual.

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

April 27, 1998

To: File for Antimony Trisulfide (Sb_2S_3) (CAS No. 1345-04-6)

From: Dan O'Brien, Toxics Unit, Air Quality Division

Subject: Initial Threshold Screening Level (ITSL) for Antimony Trisulfide

The ITSL for antimony trisulfide is 0.2 µg/m^3 based on a 24 hour averaging time.

The following references or databases were searched to identify data to determine the ITSL: AQD chemical files, IRIS, HEAST, ACGIH TLV Booklet, NIOSH Pocket Guide to Chemical Hazards, RTECS, NTP Management Status Report, EPB Library, IARC Monographs, CAS On-line and NLM/Toxline (1967 - September, 1996), CESARS, Handbook of Environmental Data on Organic Chemicals, Patty's Industrial Hygiene and Toxicology, Merck Index and Condensed Chemical Dictionary. A summary of the toxicological literature for Sb_2S_3 has been prepared by other AQD staff and documented in the AQD Interim Chemical Evaluation form dated December, 1997. In the interest of brevity, that information will not be repeated here, and the interested reader is referred to that document (in the chemical file for Sb_2S_3), and to other summary references concerning the toxicity of Sb (EPA, 1987; IARC, 1989; ATSDR, 1992; Beliles, 1994) for a complete discussion of the literature. Only points immediately relevant to the final derivation of the screening level will be addressed here.

It should be noted at the outset that some compounds of Sb (specifically Sb trioxide [Sb_2O_3] (CAS# 1309-64-4) and Sb trisulfide [Sb_2S_3] (CAS #1345-04-6)) have been found to be carcinogenic in a small number of laboratory animal studies (Wong et al., 1979; Watt, 1983; Groth et al., 1986)[1]. Other studies (Kanisawa and Schroeder, 1969; Schroeder et al., 1970; Newton et al., 1994) have not found this positive association. As a group, the studies vary widely with respect to quality, study design and route of exposure. The two studies that have produced positive evidence of carcinogenicity have both been inhalation studies, while the negative studies have been by both the oral and inhalation routes of exposure. Sb compounds have been shown to be carcinogenic in only one species (rats). The carcinogenic potential of Sb compounds may be related to the deposition and clearance of Sb from the respiratory tract; this, in turn, may depend on particle size. ATSDR (1992) speculates at length that smaller Sb particles are deposited deeper in the lung and, being relatively insoluble, are cleared more slowly. Thus, smaller particles may be in contact with pulmonary tissue for longer periods of time, leading to reactive processes typical of pneumoconiosis. So,

[1] It should be noted, when assessing the weight of evidence for carcinogenicity, that Wong et al., 1979 and Groth et al., 1986, though separate publications, report results of studies on the same group of animals. Thus, they jointly represent one positive study rather than two.

uncertainties relevant to other substances which induce pneumoconiosis and lung cancer may also be relevant to Sb compounds. It must also be noted that supporting evidence for the positive rat studies from human occupational epidemiological experience is minimal and confounded. The complete body of work has been discussed in detail elsewhere (IARC, 1989; ACGIH, 1991; ATSDR, 1992; Beliles, 1994), and will not be reviewed again here. The International Agency for Research on Cancer (IARC) has concluded that while there is sufficient evidence for the carcinogenicity of Sb_2O_3 in experimental animals, there is only limited evidence for the carcinogenicity of Sb_2S_3 in experimental animals, and that there is inadequate evidence for the carcinogenicity of both Sb_2O_3 and Sb_2S_3 in humans.

The Inhalation Reference Concentration (RfC) is given first preference as data on which to base an ITSL. This concentration can be used without modification when it has been derived previously by EPA. No RfC has been developed for Sb_2S_3 One could consider using the rat inhalation study of Groth et al. (1986) in derivation of an RfC-based ITSL, but this is problematic for a number of reasons. First, the animals in that study were exposed to Sb ore rather than pure Sb_2S_3. While Sb ore is composed principally of Sb_2S_3, it also contains other components (among them arsenic [As], a known human lung carcinogen), meaning that the health effects manifest in the study animals were essentially the product of a mixed exposure. Despite the fact that the majority of the material to which they were exposed was likely composed of Sb_2S_3, it is not possible to determine whether Sb_2S_3, or one of the other constituents of the ore, was responsible for the observed health effects. Second, the primary clinical signs in the most affected animals exposed to Sb ore were respiratory, particular lung tumors. These were found at elevated proportions above those in the controls only among the females. Notably, As concentrations were significantly higher in lungs (as well as livers, kidneys, spleens, brains and blood) of female rats than in males similarly exposed. This was not the case with respect to tissue Sb concentrations, for which there was either no significant difference between sexes, or which, in the case of lung, were significantly higher in the males. This casts further doubt on conclusions that the observed health effects were due to Sb_2S_3. Finally, the investigators in Groth's study apparently experienced substantial difficulties regulating exposure concentrations to the animals, and target exposure concentrations were only reached and maintained dependably after more than seven months of the 12 month exposure duration had already passed. Such uncertainty as to the true concentrations to which the animals were exposed makes this study unsuitable for quantitative risk assessment. A second approach would be to use the RfC for Sb_2S_3 (IRIS, 1995); it is 0.2 $\mu g/m^3$. Beliles has noted that "Sb_2S_3 results from the roasting of antimony sulfide ores (and) from air oxidation of molten Sb metal..."So, if it can be assumed that the trisulfide ore itself is unlikely to be used in industrial applications, but rather as a component in the production of Sb or Sb_2O_3, it seems likely that Sb_2S_3 would be subjected to heat processing that would drive off the sulfur. Consequently, exposure to members of the public would most likely be to the trioxide, in which case the RfC would constitute the best health-based limit available, and would be the preferred basis for the screening level for Sb_2S_3.

When adequate data for RfC calculation are not available, next preference is given to oral data for calculation of a Reference Dose (RfD) if available data do not indicate that extrapolation from the oral to the inhalation route of exposure is inappropriate. While EPA has published an RfD for metallic antimony [Sb] (IRIS, 1992), much evidence

exists (ACGIH, 1991; ATSDR, 1992; Beliles, 1994) to show that many of the most sensitive and serious effects of inhalation exposure to various antimony compounds occur in the respiratory tract. Moreover, upper respiratory irritation is a prominent clinical sign in workers exposed to antimony compounds. Thus, the existence of portal of entry effects may make an oral to inhalation extrapolation unwise for Sb, making the RfD inappropriate for use as the basis of the screening level.

Occupational Exposure Limits (OELs) [both the American Conference of Governmental Industrial Hygienists Threshold Limit Value (ACGIH-TLV) and the National Institute for Occupational Safety and Health's Recommended Exposure Level (NIOSH REL)] are available for antimony and compounds. OELs are specified in Rule 232(1)(c) as being the next most appropriate basis for derivation of the ITSL if an RfC or RfD (or long-term data to derive them) are not available or are not appropriate. The TLV is actually based not on data for the toxicity of Sb per se, but rather on the TLV for hydrochloric acid [HCl] (CAS# 7647-01-0). The link with Sb comes from consideration of the effects of the chlorides of Sb, antimony trichloride [Sb_2S_3] (CAS# 10025-91-9) and antimony pentachloride [$SbCl_5$] (CAS #7647-18-9). ACGIH (1991), citing Taylor (1966), describes slightly delayed abdominal pain and anorexia (over and above the irritant effects due to HCl) in workers exposed acutely to $SbCl_3$ in an occupational setting. They report similar but more intense effects from $SbCl_5$ exposure. In the absence of better data upon which to base the TLV, ACGIH appears to have determined that approximately 39% of the molar weight of $SbCl_5$ was due to Sb, and the rest (61%) due to Cl. Since the previously determined TLV for HCl was 7.5 mg/m^3, they simply scaled that TLV up to cover the remaining 39% of the molar weight of $SbCl_5$, making the TLV for $SbCl_5$ = 12.3 mg/m^3. Subtracting from that concentration the portion due to Cl (7.5 mg/m^3) left a TLV of ~5 mg/m^3 for the Sb component. "Because the reported effects appear to be greater than those of hydrochloric acid alone...," ACGIH appears to have then divided 5 mg/m^3 by a ten-fold uncertainty factor to obtain the final Sb TLV of 0.5 mg/m^3 on a time-weighted average. One cannot help but commend ACGIH's resourcefulness in deriving a TLV for Sb and compounds in the absence of specific Sb toxicity data.

Nonetheless, given the previously mentioned fact that processing would likely oxidize Sb_2S_3 to Sb_2O_3 prior to human exposure via ambient air, the RfC for Sb_2S_3 arguably provides a more scientifically-valid basis for the derivation of a screening level for Sb than does the TLV for Sb and compounds, which is based on HCl. Consequently, that RfC will be used as the basis of the ITSL.

Derivation of the ITSL: Applying Rule 232(1)(a), the ITSL for Sb_2S_3 equals the inhalation RfC for Sb_2S_3. Therefore:

ITSL = RfC = 0.0002 mg/m^3 x 1000µg/1mg = 0.2 $\mu g/m^3$

and per Rule 232 (2)(b), a 24 hour averaging time applies.

It should be reiterated that the appropriateness of this ITSL for Sb_2S_3 is dependent on the assumption that processing would ensure that the ultimate public exposure was to the trioxide rather than the trisulfide itself. If there is reason to believe, based on the particular process involved, that this assumption is not valid in a particular situation,

further review may be warranted to identify other toxicological data on which to base some alternative ITSL.

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